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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/691,053	Applicant(s) AGUR ET AL.	
	Examiner Marjorie A. Moran	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-509* is/are pending in the application.

4a) Of the above claim(s) *1-233,248-465 and 480-509* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *234-247 and 466-479* is/are rejected.

7)☒ Claim(s) *242* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

All rejections and objections not repeated below are hereby withdrawn.

Election/Restrictions

Applicant's election with traverse of Group VIII, claims 234-247 and 466-479 in Paper No. 15, filed 9/9/02, is acknowledged. The traversal is on the ground(s) that there would not be a serious burden to search both Groups VII and VIII. Similar arguments are set forth with regard to Groups I and II, and with regard to Groups III and IV. This is not found persuasive because the Groups are directed to separate and distinct inventions, as set forth in the Restriction Requirement. Further, it is noted that the claims of Groups I and VII recite a selector whereas the claims of Groups II and VIII do not. The claims of Groups II, IV and VIII recite a predictor, which is not recited in the claims of any of Groups I, III, and VII. A search for a system and method comprising a selector is necessarily a different search than that for a system and method comprising a predictor, or comprising only a model (Group III). In addition, a search for any one Group requires a search of nonpatent and foreign literature as well as a search of US patents. In response to the argument that that claims in various Groups have already been examined on their merits, applicant's attention is directed to 37 CFR 1.142, which states that, "Such requirement will normally be made before any action on the merits; however, it may be made at any time before final action." Further, as previously set forth in several interviews, the restriction is made to clarify the issues for examination and, hopefully, expedite agreement on allowable claims. For these reasons and those previously set forth, the examiner maintains that a search for more than a single Group would be undue, and maintains that the restriction is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-233, 248-465, and 480-509 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

An action on the merits of elected claims 234-247 and 466-479 follows.

Claim Objections

Claim 242 is objected to because of the following informalities. In line 2, a comma or semicolon should be inserted after "tumor". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 234-247 and 466-479 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Line 2 of each of claims 244 and 476 recites "pharmacokinetic, pharmacodynamic, ..." but do not recite if these are methods, models, interactions, reactions, etc., therefore the claims are indefinite.

Claims 246 and 478 similarly recite "patient specific drug pharmacokinetic, pharmacodynamic ..." but does not recite if these are interactions, reactions, parameters, models, etc., therefore the claims are indefinite.

Claims 234 and 466 recite a narrower limitation and a broader limitation. See above regarding narrower limitations and broader limitations in the same claim. The broader limitation is "treating cancer using drugs", the narrower limitation is "chemotherapy".

Claims 240 and 472 recite the phrase "a set control functions that are adapted" in lines 1-2. It is unclear if applicant intends --a set of control functions which are adapted-- or --set control functions that are adapted-- or --a control function that is adapted--. As it is unclear what limitation applicant intends by this phrase, the claims are indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicant's arguments with respect to claims 234-247 and 466-479 have been considered but are moot in view of the new ground(s) of rejection.

Claims 234-235, 246-247, 466-467, and 478-479 are rejected under 35 U.S.C. 103(a) as being unpatentable over ILIADIS et al. (IDS ref: Computers and Biomed. Res. (2000), vol. 33, pages 211-226).

Claim 234 recites a computer system comprising a cancer system model, a treatment protocol generator, a system model modifier, and a selector. Claim 466 recites a computer-implemented method of recommending an optimal treatment protocol for treating cancer with drugs comprising creating a cancer system model, enumerating a plurality of treatment protocols for cancer treatment, modifying the system model based on an individual's parameters, selecting an optimal treatment protocol, and recommending the optimal treatment. Claims 235 and 467 limit the system model to further comprise a process model of cancer development and a treatment model that models the effects of treating cancer with drugs. Claims 246-247 and 478-479 limit the individual's parameters.

ILIADIS teaches a system and method for recommending an optimal treatment protocol for chemotherapy of tumors (cancer) wherein a cancer system model comprising PK and PC data is generated (pp. 213-214), a plurality of treatment protocols enumerated (p. 218), an optimal treatment protocol selected (p. 219), and recommended (p. 223: Protocols used...). ILIADIS also teaches that his model may be modified by patient parameters, such as body surface area, size of tumor, and tumor cell population (p. 217: The Data). As ILIADIS teaches a method which requires a cancer system model, a treatment protocol generator, a system model modifier, and a selector, he necessarily teaches a system comprising a cancer system model, a treatment protocol generator, a system model modifier, and a selector. ILIADIS does not specifically teach recommending an optical treatment protocol for a specific individual.

It would have been obvious to one of ordinary skill in the art at the time of invention to have used the system and method of ILIADIS to recommend an optimal treatment protocol for cancer in an individual where the motivation would have been to determine optimal dosage protocol based on a patient's body size and tumor load, as suggested by the teaching of ILIADIS for inclusion of patient and tumor parameters in his model.

Claims 234-242, 244-247, 466-474, and 476-479 are rejected under 35 U.S.C. 103(a) as being unpatentable over ILIADIS et al. (IDS ref: Computers and Biomed. Res. (2000), vol. 33, pages 211-226) in view of PERIERA et al. (IDS ref: Frontiers Med. Biol. Eng. (1995), vol. 6 (4), pages 257-268).

Claims 234-235, 246-247, 466-467, and 478-479 recite a computer system and computer-implemented method of recommending an optimal treatment protocol for treating cancer with drugs, as set forth above. Claims 236 and 468 limit the process model to incorporate a distribution of cycling and quiescent cells. Claims 237 and 469 limit the system and method to ones wherein a tumor cell cycle is divided into particular compartments and sub-compartments and a cell entering a compartment is constrained to always enter a first sub-compartment of a compartment. Claims 238 and 470 limit the model to be one which traces development of cancer cells by calculating the number of cells in each sub-compartment. Claims 239 and 471 limit the system and method to comprise a probability vector which determines the fraction of cells leaving a sub-compartment to move to a first sub-compartment in another compartment. Claims 240 and 472 limit the system and method to comprise control functions comprising the age of cells, state of a current population and associated environment. Claims 241 and 473 limit the system and method to comprise a tumor model comprising a combination of a plurality of groups of cells. Claims 242 and 474 limit the system and method to comprise calculations for a number of cells in each sub-compartment, for each step. Claims 244 and 476 limit the system and method to comprise PK and PD, cytostatic effects, cytotoxic effects, and other effects on cell disintegration. Claims 245 and 477 limit the system and method to comprise a dose-limiting toxicity.

ILIADIS teaches and makes obvious a system and method for recommending an optimal treatment protocol for chemotherapy of tumors (cancer) wherein a cancer system model comprising PK and PC data is generated (pp. 213-214), a plurality of treatment protocols enumerated (p. 218), an optimal treatment protocol selected (p. 219), and recommended (p. 223: Protocols used...), as set forth above. ILIADIS further teaches inclusion of cytotoxic effects and calculation of a dose-limiting toxicity (page 215 and Figure 2). ILIADIS does teach a compartmental model (p. 213), but does not teach cell distribution or entry into specific cellular compartments in his model.

PERIERA teaches a method of designing /recommending optimal drug protocols for treatment of cancer wherein a model includes cancer cell population growth and PK dynamics (abstract). PERIERA specifically teaches selection of an optimal patient-tailored drug-dose schedule (p. 264), and teaches organizing a tumor cell population into various compartments, which include a G_0 (resting or quiescent) phase and various cycling phases (p. 260). PERIERA teaches various sub-compartments of his compartments, calculates the number of cells that transition from one compartment (or sub-compartment) to another, and the number of cells in each compartment at particular steps (pp. 260-261, 265-266, and Figure Figure 2). PERIERA also teaches that his algorithms may be applied in methods where cell population growth and PK are associated in the same model.

It would have been obvious to one of ordinary skill in the art at the time or invention to have included all of the cell compartment parameters and calculation of PERIERA in a method and system for recommending optimal treatment protocols for cancer in an individual patient, as taught by ILIADIS, where the motivation would have been to make the model in the method and system more precise and realistic, as suggested by the teachings of PERIERA that a model which includes both cellular and PK parameters gives both more precise and more meaningful

(i.e. realistic) results (p. 267). One skilled in the art would reasonably expect success in incorporating the cell compartment parameters and calculations of PERIERA in the method and system of ILIADIS because PERIERA teaches that PK calculations and parameters, such as those taught by ILIADIS, may be combined with cell population growth calculations, and because ILIADIS and PERIERA teach similar method of determining optimal protocols for treatment of cancer with drugs.

Claims 243 and 475 are rejected under 35 U.S.C. 103(a) as being unpatentable over ILIADIS et al. (IDS ref: Computers and Biomed. Res. (2000), vol. 33, pages 211-226) in view of PERIERA et al. (IDS ref: Frontiers Med. Biol. Eng. (1995), vol. 6 (4), pages 257-268) as applied to claims 234-242, 244-247, 466-474, and 476-479, above, and further in view of LEMELSON (US 5,919,135).

The claims recite a computer system and computer-implemented method of recommending an optimal treatment protocol for treating cancer with drugs, wherein cells enter compartments, as set forth above. Claims 243 and 475 limit the model to include a spatial structure of the tumor.

ILIADIS and PERIERA make obvious a compartmental system and method for recommending an optimal treatment protocol for chemotherapy of tumors (cancer), as set forth above. ILIADIS and PERIERA do not teach a spatial structure of a tumor in their model.

LEMELSON teaches computer modeling of blood flow and drug dispersion during infusion of cytotoxic drugs for cancer treatment, wherein his model includes a spatial structure of the tumor (abstract, Figure 4, and col. 4, lines 5-20).

It would have been obvious to one ordinary skill in the art at the time of invention to have included spatial coordinates of a tumor, as taught by LEMELSON, and the calculations for

blood flow, diffusion, and cytotoxicity, in the method of system of ILIADIS and PERIERA where the motivation would have been to more accurately simulate and predict an optimal dosage/treatment regimen for a patient based on the size and shape of a tumor and the diffusion and clearance parameters of an infused drug, as suggested by the teaching of ILIADIS that circulating drug concentrations are a parameter in his model (p. 219), and the teachings of all that minimization of general toxicity while maximizing tumor kill rate is a desired goal of chemotherapeutic treatment.

Conclusion

Claims 234-247 and 466-479 are rejected; all other claims are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to an LIE, Tina Plunkett, whose telephone number is (703) 305-3524.

November 17, 2002

MARJORIE MORAN
PATENT EXAMINER
Marjorie A. Moran